REMARKS/ARGUMENTS

Claims 1-7 and 9-19 are pending in the captioned application. Claims 5 and 13 are withdrawn as related to non-elected species. Applicants have amended claims 1, 3-6, 9, 11-13 and 16-18. Applicants have also cancelled claims 2 and 14-15. Claims 1, 3-7, 9-13 and 16-19 are therefore currently pending. Applicants respectfully request reconsideration and allowance of the claims in view of the amendments and the arguments below.

Applicants first thank the Examiner for the telephone interview conducted on June 24, 2009. In the following remarks, consideration has been given to the discussion during the interview.

Applicants submit that the amendments are fairly based on the specification and do not introduce new matter. With regard to claim 1, the invention described that the function of one or more effector from a library of effector nucleic acid sequences can be assigned through an innovative process (cee paragraph [0082] of the published US patent application, i.e. "*[B]y collecting data from a large number of triplets where unknown elements are tested in combination with known elements and selecting triplets in which there is an interaction between all three components it is possible to assemble networks of functional linkages which yield information on the biological function of previously uncharacterised elements.*") .

In the first step of claim 1, the distribution pattern of a detectable label which is expressed from one of a group of indicator nucleic acid sequences is determined in

cells that express one of the effector nucleic acid sequences, both in the presence and the absence of one of a group of chemical modulators that affect distribution of the detectable label (see paragraph [0076], where a round of screening is carried out in which effector nucleic acid sequences are transfected into cells expressing the detectable fusion protein (indicator) in the absence and presence of the modulator).

The process is repeated with additional effector nucleic acid sequences from the library of effector nucleic acid sequences in step (ii) of claim 1 (see paragraph [0077]). The process may also be repeated with additional chemical modulators and indicators (see paragraphs [0077] and [0081]) in step (iv) of claim 1. The distribution data of the detectable label from all combinations of said effectors, modulators and indicators is analyzed to derive functional linkages among the effectors, modulators and indicators (claim 1, step (iii); see paragraph [0081]). The process is repeated with different combinations of effector nucleic acid sequences, chemical modulators and indicator nucleic acid sequences until a function is assigned successfully to the one or more effector nucleic acid sequences (claim 1, step (iv); see paragraph [0082], e.g., "*networks of functional linkages . . . yield information on the biological function of previously uncharacterised elements*", and "*consequently yields information on the possible biological activities of the modulator and effector of the first triplet*").

Applicants submit that no new matter is introduced by the amendments to claim 1. Furthermore, the other claim amendments are introduced merely to improve the consistency of the claims and do not introduce any new matter either.

The claims are rejected under 35 U.S.C. §112 by the Examiner in paragraph 7 of the Officer action as containing new matter. However, Applicants submit that the rejected claim language has now been removed from the claims. Thus the rejection should be withdrawn.

The claims stand rejected under the 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement (paragraph 8 of the Office action). Applicants respectfully disagree.

Applicants submit that the claimed invention relates to cell-based approaches for functional screening of nucleic acid sequences as exemplified by claim 1. The method offers unique advantages over prior art. It provides methods for functional screening in which assays are generated in concert with screening in an iterative process which expands the scope of biological coverage with each iteration and which uses image-based analysis to yield data at sub-cellular resolution (see paragraph [0023]) The method takes advantage of the fact that many cellular proteins exhibit a characteristic cellular localization and in many cases change their cellular localization in response to certain stimuli. Consequently, given collections of nucleic acid sequences (i.e. effector or indicator) and of chemical compounds (i.e., modulators), it is possible to generate pairings of one nucleic acid sequence with one modulators to produce a specific cellular localization of a marker coupled to the product of the nucleic acid sequence. Such pairings may then be used as diagnostic assays for testing against other collection members (i.e., effectors) and thus build up clusters and linkages therebetween. In this way, using some members of each collection which are

of known function, it is possible to assign function to previously uncharacterized elements by linkage to known elements.

Thus, the current invention relates to a functional screening method to assign functions to functionally unknown genetic elements. It does not claim any genetic elements themselves as in *University of California v. Eli Lily and Co.*, 43 USPQ2d 1398 (1997). Nor does the claimed invention attempts to claim a method for blocking a specific gene activity as in *Univ. Rochester v G.D. Searle & Co.*, 358 F.3d 916 ((Fed. Cir. 2004). Here, a function of a genetic element (i.e., effector) is attributed by a process that connects the effector with some modulators and further effectors, and through the networks of functional linkages, a function for the effector is deduced when the function of one of the effectors in the network is known (see paragraph [0082]).

Applicants submit that the specification and the drawings fairly describe the claimed invention. Figures 3, 4 and 5 and accompanying text described the functional screening method in detail. Once a subcellular localization pattern is established, further rounds of screening can be performed with different effectors or modulators. Many three-way combinations can be tested (see paragraph [0081]). Biological function of previously uncharacterized effectors can be obtained through the collection of data including various triplet combinations (see paragraph [0082]). As states in the specification, "the process inherently generates cellular assays [thus] the method has advantages over previously used approaches in that it does not require either prior knowledge of biological activities or pre-existing cell assays . . ." (see

paragraph [0078]). Given the above description of the invention, Applicants submit that the invention is predictable and well described.

The claims stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In response, Applicants first submit that claim 1 has been amended rendering many of the rejections here moot. Applicants have also amended many of the claims to be consistent with the newly amended claim 1. Thus the 35 U.S.C. §112, second paragraph rejection should be withdrawn.

The claims stand rejected under 35 U.S.C. §103(a) as being unpatentable over Thastrup in view of Bastiaens, and Rolls and Diamond. Applicants respectfully disagree.

In response, Applicants submit that Thastrup teaches use of imaging to measure changes in the distribution of a luminophore, specifically GFP, within cells where the GFP is fused to a protein of known function, wherein changes in distribution of the fusion protein provides information relating to an external influence, specifically a substance having biological activity, on a cell response. Consequently Thastrup teaches a screening method for determining the activity of a substance, typically a candidate drug, against a known biological process using a GFP fusion to a DNA sequence coding for a protein of known function. However, Thastrup teaches the use of only two components;

(i) a GFP fusion protein (e.g. PKA-GFP), which is the equivalent of the indicator in the present invention; and

(ii) a test substance (e.g. forskolin), which is the equivalent of the modulator in the present invention.

The method of Thastrup provides means to determine whether a substance having biological activity is active against a chosen known cellular process, e.g. to determine if a drug candidate compound inhibits a cellular signalling pathway which is the focus of a therapeutic program. In this aspect the method of Thastrup conforms to standard drug screening methodology, i.e. providing an assay against which multiple compounds may be individually tested in parallel for activity.

Since the method of Thastrup utilizes only two components, the function of one of which by definition has to be known, the method does not teach or motivate the method of the present invention in providing means to generate networks of functional linkages using combinations of indicators, modulators and effectors in order to assign function to an effector.

Because Thastrup does not teach or motivate the method of the present invention, addition of the teachings of Bastiaens, Rolls or Diamond which relate only to the use of GFP fusion proteins to measure cellular events (as described by Thastrup) and to the use of chemical libraries for drug screening (as described by Thastrup) is redundant and therefore does not render the claims unpatentable. .

Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of claims 1, 3-7, 9-13 and 16-19.

Early and favorable consideration is respectfully requested.

Respectfully submitted,

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